REMARKS

Applicants respectfully request reconsideration of the present application in view of the reasons that follow.

I. Status of the Claims

Claims 26, 27, 29, and 30 are canceled without prejudice or disclaimer.

Claims 24, 28, and 31 are amended. The amendments generally make terminology consistent among the claims and correct minor typographical errors. No new matter is being added.

Upon entry of the amendments, claims 24, 25, 28, and 31 will be pending and subject to examination on the merits.

II. Objection to the Claims

Claims 24-28 and 31 are objected to for the reasons detailed in paragraphs 7-10 of the Office Action. The amendments render moot these objections. Accordingly, Applicants respectfully request withdrawal of these objections.

III. Claim Rejections under 35 U.S.C. 112, second paragraph

Claims 26 and 29 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Specifically, the Office Action states that claims 26 and 29 are indefinite for reciting "from 0.16 mg/mL inclusive" and "according to anyone of claim 16."

While not acquiescing to the propriety of the rejections, Applicants have amended the claims to render moot these grounds of rejection. Thus, Applicants respectfully request withdrawal of these rejections.

IV. Claim Rejections under 35 U.S.C. 103

Claims 24-31 stand rejected as allegedly obvious over Borque *et al.*, EUR. J. CLIN. CHEM. CLIN. BIOCHEM. 12:869-74 (1993) in view of U.S. Patents Nos. 4,362,531 (de Steenwinkel), 6,447,774 (Metzner), and 5,80,679 (Schmitdberger). According to the Office Action, Borque discloses a turbidimetric immunoassay that meets Applicants' claim recitations but for the omissions of (i) a basic amino acid addition and (ii) specifying the antibody concentration employed in the claimed assay. The secondary references are cited to remedy this deficiency. Applicants respectfully request traverse this ground of rejection.

Applicant's claimed turbidimetric assay measures a plurality of lipoprotein(a) phenotypes that the primary reference explicitly discounts for contributing "only slightly to the size heterogeneity." Borque at page 872, lines 15-17. This is achieved by using a high antibody concentration, as recited, along with the prescribed level of a arginine, which circumvents the influence of isoform variation in measurements attributable to phenotypic variations. *See* specification at page 2, lines 24-26.

The references of record do not suggest to one of skill in the art the use of "arginine" in an amount of "12% or greater." de Steenwinkel employs a chaotropic or chaotropic-like agent is used to ***reduce*** interferences due to non-specific protein-protein interactions. On the other hand, the claimed method employs arginine to circumvent the influence of variations in measurement values attributable to phenotypic differences as the specification of the present application describes. In other words, arginine ***increases*** protein-protein interactions. The variability of a measurement value cannot be attributed to the interferences due to non-specific protein-protein interactions. Accordingly, it cannot be predicted that a chaotropic or chaotropic-like agent disclosed in de Steenwinkel would useful for circumventing the influence of variations in measurement values attributable to phenotypic differences.

de Steenwinkel lists a variety of possible chaotropic agents: guanidine, guanidinium hydrochloride or thiocyanate, sodium and ammonium thiocyanates, urea and various detergents are exemplified. de Steenwinkel also lists a variety of possible chaotoropic-like agents: sodium chloride, ethylenediamine tetra-acetic acid (EDTA), lithium nitrate, lithium

chlorate, lithium isocyanate, lithium bromide, sodium bromide, potassium bromide, potassium thiocyanate, calcium chloride, lithium chloride, and lithium iodide are exemplified.

Yet "arginine" is not listed. The exemplary chaotropic agents would not be useful replacements for arginine in the claimed method.

Metzner teaches that known chaotropic agents include arginine. But one of skill in the art would not be motivated to use arginine because nothing in the references of record suggests that arginine can be used to circumvent the influence of variations in measurement values attributable to phenotypic differences. Moreover, use of "arginine" results in unexpected results, that is, the ability to detect phenotypic variants of lipoprotein(a). Indeed, as noted above, the chaotropic agents listed by de Steenwinkel would be unsuitable for use in the claimed method.

The Office Action notes that that Barque discloses data that show that results obtained using latex turbidimetric method correlates with results obtained by ELISA (Figs. 3c and 3d). However, the correlation coefficient is relatively low – r^2=0.956 for Figs. 3c and 3d. Barque acknowledges this low correlation: "we found slopes significantly different from 1.0, indicating that there was no transferability among the different methods." Barque at pg. 871, right col., 1st ¶. The claimed method, on the contrary, results in a high correlation coefficient: r^2 is 0.973 when arginine is used at 10%; r^2 is 0.998 when arginine is used at 15%; and r^2 is 1.000 when arginine is used at 17%. The difference of r^2 between 0.973 and 0.956 is considerable difference in the field of diagnosis. It is possible that the low correlation is due to variations in measurement values attributable to phenotypic differences.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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